Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Michael S. Greenfield on May 20, 2010.

Claims 1, 15, 20, 21, 22, and 24 are amended as follows:

1. (Currently Amended) A pneumococcus type 5 capsular polysaccharide, wherein the polysaccharide is aminated on the terminal aldehyde group and exhibits

(i) a carbon (13C) NMR spectrum having

(a) no resonance signal between 13 and 14 ppm inclusive;

(b) no resonance signal between 11.5 and 12.5 ppm, inclusive; and

(c) a resonance signal located between 17 and 18 ppm inclusive, characteristic of N-acetylated quinovosamine, the intensity of which is increased in comparison with the resonance signal located between 17 and 18 ppm, inclusive, in the (13C) NMR spectrum of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours;

(ii) an HPAEC-PAD chromatogram obtained by elution from a anion-

exchange column in an 18 mM sodium hydroxide solution at a flow rate of 1 ml/min for 15 min of monosaccharides derived from hydrolysis of said polysaccharide having:

(a) no peak between fucosamine and pneumosamine peaks; and

(b) a peak located immediately after the pneumosamine peak characteristic of quinovosamine, the intensity of which is increased in comparison with the equivalent peak in the HPAEC-PAD chromatogram of a pneumococcus type 5 capsular polysaccharide obtained after reductive amination in the presence of sodium cyanoborohydride at pH 8 for 48 hours;

or

(iii) both,

and wherein the anion-exchange column consists of a support based on polystyrene and sulfonated divinylbenzene having a degree of cross-linking of 55% and latex microbeads with quaternary ammonium groups; wherein the latex microbeads have a degree of cross- linking of 5% and the diameter of 400 nm.

15. (Currently Amended) A method for producing an aminated pneumococcus type 5 capsular polysaccharide according to claim 8, the method comprising (i) reacting a pneumococcus type 5 capsular ~~according to which (i) the~~ polysaccharide ~~is reacted~~ with

an agent for reducing a ketone function, (ii) fragmenting the reduced polysaccharide ~~is fragmented~~, and (iii) reductively aminating the reduced and fragmented polysaccharide ~~is subjected to a reductive amination~~.

20. (Currently Amended) ~~A method for producing a conjugate of formula Ps-CH2-NH-P, according to which a~~ The method according to Claim 15 wherein the reductive amination of ~~is used, in which~~ the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is conducted with ~~coupled by reductive amination with~~ a carrier polypeptide (P), wherein the Pneumococcus type 5 capsular polysaccharide produced is a conjugate of formula Ps-CH_2-NH-P.

22. (Currently Amended) [A] The method according to claim 15 wherein ~~for producing a conjugate of formula Ps-CH2-NH-L-P, in which~~:

(i) (a) ~~a method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by~~ the reductive amination is conducted with ~~to~~ a linking agent (L) having at least one free amine function so as to form an aminated and activated polysaccharide of formula Ps-CH_2-NH-L, and

(b) further comprising coupling the activated polysaccharide ~~is coupled~~ to a carrier polypeptide (P) in order to obtain an aminated pneumococcus type 5 polysaccharide ~~the conjugate~~ of formula Ps-CH_2-NH-L-P; or, alternatively,

(ii) ~~the method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by~~ the reductive amination is conducted with ~~to~~ an activated carrier polypeptide of formula L-P, wherein L is a linking agent having at least one free amine function, in order to obtain an aminated pneumococcus type 5 polysaccharide ~~the conjugate~~ of formula Ps-CH2-NH-L-P.

24. (Currently Amended) [A] The method according to claim 15, wherein ~~for producing a conjugate of formula Ps-CH2-NH-S-L'-P, in which~~:

(i) the ~~method according to Claim 15 is used, wherein the reduced and fragmented pneumococcus type 5 capsular polysaccharide (Ps) is coupled by~~ reductive amination is conducted with ~~to~~ a spacer (S) having at least one free amine function so as to form an aminated and derivatized polysaccharide of formula Ps-CH_2-NH-S, and further comprising

(ii) (a) coupling the derivatized polysaccharide ~~is coupled~~ with a linking agent (L') in order to obtain an activated polysaccharide of formula Ps-CH_2-NH-S-L', then the activated polysaccharide is coupled with a carrier polypeptide (P), in order to obtain an aminated pneumococcus type 5 polysaccharide ~~the conjugate~~ of formula Ps-CH_2-NH-S-L'-P; or, alternatively,

(b) coupling the derivatized polysaccharide ~~is coupled~~ with an activated carrier polypeptide of formula L'-P, wherein L' is a linking agent, in order to

obtain an aminated pneumococcus type 5 polysaccharide ~~the conjugate~~ of formula Ps-CH_2-NH-S-L'-P.

Withdrawn claims 11-14, 19, 21, 23, and 25-29 are cancelled.

Detailed Action

This office action is a response to applicant's communication submitted March 5, 2010 wherein claim 8 is amended. This application claims benefit of foreign application 60/442154, filed January 22, 2003.

Claims 1, 8, 10, 15-18, 20, 22, 24, 30, and 31 are pending in this application.

Claims 1, 8, 10, 15-18, 20, 22, 20, 30, and 31 as amended are examined on the merits herein.

Reasons for Allowance

Applicant's amendment and arguments, submitted March 5, 2010, with respect to the rejection of instant claims 1, 8, 10, 30, and 31 under 35 USC 103(a) for being obvious over Moreau in view of Jansson et al., has been fully considered and found to be persuasive to remove the rejection as Jansson et al. does not provide any clear teaching that would lead one of ordinary skill in the art to reduce the carbonyl group of a pneumococcus capsular polysaccharide conjugate vaccine. Therefore the rejection is withdrawn.

The requirement for restriction issued August 24, 2006, is withdrawn in view of the allowability of the elected claims 1, 8, 30, and 31. Withdrawn claims 15-18, 20, 22, and 24 are rejoined and examined on the merits herein.

Currently claims , 8, 10, 15-18, 20, 22, 24, 30, and 31 are pending in this application and have been examined on the merits herein. Applicant's amendment and arguments submitted March 5, 2010, and the enclosed examiner's amendment, are seen to be persuasive to remove all rejections of record in the previous office action and place the application in condition for allowance. Reasons for allowance are as follows:

The claimed invention is seen to be adequately described and enabled by the specification as originally filed. Therefore the claims meet the requirements of 35 USC 112.

Furthermore the claimed invention is seen to be novel and non-obvious over the prior art. The claims are directed toward certain specific types of aminated pneumococcal type 5 capsular polysaccharide. The limitations of claim 1 recite certain specific spectroscopic and chromatographic properties of the composition. According to the instant specification, (p. 6 lines 1-20) the ^{13}C NMR peak between 17 and 18 ppm denotes the desired product which is a reduced quinovosamine-containing polysaccharide conjugate, and the peak between 13 and 14 ppm (which is absent in the claimed products) denotes the presence of an uncharacterized impurity known as compound X which is present in samples of pneumococcal type 5 capsular polysaccharide which have been subjected to long reductive amination reactions according to standard prior art methods. P. 6 lines 22-38 of the specification furthermore indicate that a chromatographic peak between fucosamine and pneumosanine in a hydrolysate of monosaccharides from said polysaccharide is also indicative of compound X. Therefore the absence of these spectroscopic or

chromatographic peaks indicates that the impurity "compound X" is not present in the composition. Furthermore pp. 12-14 of the specification indicates that the lack of a ^{13}C resonance signal between 11.5 and 12.5 ppm and the increased quinovosamine chromatographic peak are indicative of a product prepared by the second method described in the specification, namely reductive amination of the type 5 pneumococcal capsular polysaccharide with prior reduction and fragmentation, as opposed to the first method, which is an optimized prior art reductive amination without the prior reduction step. Therefore the polysaccharides described in claim 1 cannot have been prepared by simple reductive amination without a ketone reduction step.

Similarly, the substructure recited in instant claim 8 requires that position A be CHOH, while the equivalent position in the native pneumococcus type 5 capsular polysaccharide is a ketone. Therefore any pneumococcus type 5 capsular polysaccharide according to claim 8 must also have been subject to a reduction step.

These required reduction steps are not known in the prior art. While Moreau (US patent 6596861, cited in previous action) discloses a method for reductively aminating a pneumococcus type 5 capsular polysaccharide in under 4 hours, which is expected to produce a composition free of impurities and substantially similar to that produced by the “first method” recited on p. 4 lines 19-25 of the specification, this method would not be expected to produce a reduced polysaccharide of the type produced by the “second method" described on p. 4 lines 27-35 of the specification in which the position A is CHOH, the ^{13}C NMR peak between 11.5 and 12.5 is absent, and the quinovosamine

chromatographic peak is increased. Thus the disclosure of Moreau does not anticipate the claimed invention.

Furthermore, it would not have been obvious to one of ordinary skill in the art at the time of the invention to add a ketone reduction step either before or after the reductive amination according to Moreau et al. While Jansson et al. (Reference of record in previous action) briefly discusses a reduced pneumococcus type 5 capsular polysaccharide and speculates that it might be advantageous to use such a reduced polysaccharide in a vaccine if it possesses immunological activity, this statement is purely speculative and there is no reason to believe that the product actually possesses similar immunological activity. Therefore one of ordinary skill in the art would not have had a reasonable expectation of success in making a reduced polysaccharide conjugate according to the claims, as its immunological activity and fitness for use as a vaccine would be unknown and unpredictable.

Therefore the claims meet the requirements of 35 USC 102 and 103.

Accordingly, Applicant's amendment submitted March 5, 2010, and the enclosed examiner's amendment, are sufficient to remove all rejections made in the prior office action as discussed above and to place the application in condition for allowance.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled, "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
5/20/2010